Claims 20, 24, 26, and 29 stand rejected under 35 U.S.C. § 112, second paragraph. Claims 1-3, 6-8, 17, 19-22, 29, 30, and 34-37 stand rejected under 35 U.S.C. § 102(e) and (f). Claims 23, 24, and 26 stand rejected under 35 U.S.C. § 102(b). Claims 9-11, 14-16, 23, 24, 26-28, 34-38, 42-46, 48, and 49 stand rejected under 35 U.S.C. § 103(a). Claims 1-3, 6-11, 14-17, 19-24, 26-30, 34-38, 42-46, and 48-49 stand rejected under the judicially-created doctrine of obviousness-type double patenting.

**Formal Matters**

The Examiner objected to the specification because of an informality involving the indication of inventorship on the title page. (Office Action mailed December 17, 2002, page 3.) Applicants thank the Examiner for bringing this error to their attention. Applicants have amended the title page to conform to the declaration.

The Examiner objected to claim 43 because of an informality involving line 3. (*Id.*, page 4.) Applicants have amended claim 43 to delete the word "at" following the word "containing" as suggested by the Examiner.

The Examiner also advised that if claims 4 and 12 are allowable, claims 5 and 13, respectively, will be objected to as being substantial duplicates thereof. (*Id.*) Applicants have amended claim 4 to depend from new claim 57, which incorporates the limitations of cancelled claim 5. Applicants have also amended claim 12 to depend from claim 13 according to the Examiner's suggestion.

No new matter was added by these amendments.

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1300 I Street, NW
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202.408.4000
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**Priority**

The Examiner acknowledged Applicants' claim for priority based on application FR 95 02117 filed February 23, 1995, in France by inventors Crouzet, Scherman, Cameron, and Wils. (*Id.*, page 2.) The Examiner, however, cites M.P.E.P. § 201.13 for the proposition that a claim for priority under 35 U.S.C. § 119(a)-(d) cannot be based on application FR 95 02117 because the instant application was filed by inventors Cameron and Blanche.

M.P.E.P. § 201.13 states in relevant part:

> The conditions, for benefit of the filing date of a prior application filed in a foreign country, may be listed as follows:
>
> . . .
>
> (B) The foreign application must have been filed by the same applicant (inventor) as the applicant in the United States, or by his or her legal representatives or assigns.
>
> . . .

Applicants respectfully submit, however, that inventorship analysis under M.P.E.P. § 201.13, which is based on the provisions of 35 U.S.C. § 119, should be consistent with inventorship analysis under M.P.E.P. § 201.08 (Continuation-in-Part Application), which is based on the provisions of 35 U.S.C. § 120. M.P.E.P. § 201.08(A) states that there must be "at least one common inventor" in order for a continuation-in-part application to claim the benefit of the filing date of an earlier nonprovisional application. In Applicants' view, there is no substantive difference between the language of 35 U.S.C. § 119 ("An application for patent for invention filed in this country by any person who has . . .") and the language of 35 U.S.C. § 120 (". . . which is filed by

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an inventor or inventors named in the previously filed application . . .") that could justify such different treatment of foreign and domestic priority claims.

Applicants respectfully request the reconsideration of their claim to the benefit of the filing date of application FR 95 02117.

The Examiner further contends that Applicants have not complied with one or more conditions for receiving the benefit of an earlier filing date under U.S.C. § 120. (Office Action, page 2.) In particular, the Examiner requests that 1) the status of application 09/655,728 be updated and 2) application 08/894,511 be identified as being a 371 application of PCT/FR96/00274 not published in English. (*Id.*)

Applicants have amended the specification accordingly.

The Examiner also alleges that, with respect to the subject matter of instant claims 4, 12, 18, 25, 31-33, 39-41, 47, and 50-54, none of the priority applications describe using the specific minicircles, plasmids, or strains recited, nor the method of production of minicircles where both the minicircle region and the remaining section of the plasmid comprise a triple helix binding region. The Examiner also alleges that, with respect to the subject matter of instant claims 9-11, 14-16, 23, 24, 26-28, 42-44, 48, and 49, none of the priority applications disclose using attL or attR sequences as the repeated sequences flanking the expression cassette, and excisionase in addition to integrase for resolution. Lastly, the Examiner alleges that, with respect to the subject matter of instant claims 38 and 46, none of the priority applications disclose using the pBAD promoter for controlling expression of the integrase.

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Applicants' respectfully submit that the instant application is a continuation-in-part application of U.S. Patent No. 6,492,164 and includes claims based on both the original specification and on newly disclosed subject matter. As such, any subject matter disclosed in the priority applications is entitled to the benefit of the earlier filing dates, while newly disclosed subject matter is entitled to the benefit of the filing date of the instant application.

**The Claims Are Definite**

The Examiner rejected claims 20, 24, 26, and 29 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. (Office Action, page 5.) According to the Examiner the phrase "tRNA suppressor (supPhe)" in claims 20 and 26 is indefinite because it is unclear whether the claim is directed to any tRNA suppressor or only to a supPhe suppressor.

This rejection is moot with respect to claim 20, which has been cancelled. Applicants believe that claim 26, as-filed, clearly indicates that the marker gene is either a gene for kanamycin resistance or the supPhe tRNA suppressor. Solely to advance prosecution, however, Applicants have amended claim 26 to remove any possible ambiguity.

The Examiner also asserts that there is no antecedent basis for the limitations "said polynucleotide" in line 3 of claim 24, and "the recombinant DNA" in line 1 of claim 29.

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Applicants have amended claim 24 to provide proper antecedent basis. The rejection of claim 29, which has been cancelled, is moot.

For the reasons above, Applicants respectfully request the withdrawal of the rejection of 20, 24, 26, and 29 under 35 U.S.C. § 112, second paragraph.

**The Claims Are Not Anticipated**

The Examiner rejected claims 1-3, 6-8, 17, 19-22, 29, 30, and 34-37 under § 102(e) as allegedly being anticipated by Crouzet et al. (U.S. Patent No. 6,143,530) or Crouzet et al. (U.S. Patent No. 6,492,164) ("collectively, "the Crouzet patents"), and under § 102(f) as allegedly claiming subject matter that was not invented by the Applicants. (Office Action, page 6.)

The cancellation of claims 1-3, 6-8, 17, 19-22, 29, 30, and 34-37 renders this rejection moot.

The Examiner rejected claims 23 and 24 under § 102(b) as allegedly being anticipated by Black (Gene 46: 97-101, 1986). (*Id.*) According to the Examiner, Black discloses a plasmid comprising attR and attL sequences flanking an expression cassette, wherein the expression cassette is the tetracycline or ampicillin resistance gene in "one part of the cointegrate" or any of the λ genes of "the other part of the cointegrate." (*Id.*)

Applicants respectfully traverse. The instant claims recite a plasmid comprising an expression cassette positioned between attL and attR, and a plasmid with a selection marker gene that is outside the expression cassette. The application makes it clear that an "expression cassette" contains "a gene of interest under the control of a

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transcription promoter and a transcription terminator active in a mammalian cell." *See, e.g.*, claim 9. Neither the antibiotic resistance genes nor any of the λ genes in Black's plasmid has these properties. In fact, the instant application makes it clear that antibiotic resistance genes, for example, are selectable markers, not genes of interest. Moreover, neither the antibiotic resistance genes nor the λ genes are "under the control of a transcription promoter and a transcription terminator active in a mammalian cell." *See, e.g.*, ¶ 5. Thus, Applicants assert that Applicants' vectors are patentably distinct from those disclosed by Black and respectfully request that the Examiner withdraw the rejection of claims 23 and 24 under § 102(b).

The Examiner rejected claims 23, 24 and 26 under § 102(b) as allegedly being anticipated by Peredelchuk et al. (Gene 187 (2): 231-238, 18 March 1997). According to the Examiner, Peredelchuk discloses plasmids comprising an expression cassette, specifically one for chloramphenicol acetyltransferase (*cat*), positioned between λ attR and attL sequences. (Office Action, page 7.)

Again, Applicants respectfully traverse. The instant claims recite a plasmid comprising an expression cassette positioned between attL and attR, and a plasmid with a selection marker gene that is outside the expression cassette. The application makes it clear that an "expression cassette" contains "a gene of interest under the control of a transcription promoter and a transcription terminator active in a mammalian cell." *See, e.g.*, claim 9. In order to force the round peg of Peredelchuk into the square hole of claims 23, 24 and 26, the Examiner asserts that the *cat* gene has these properties. As an initial matter, the *cat* gene, although sometimes used to measure the

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1300 I Street, NW
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efficiency of mammalian cell transfection, is clearly an antibiotic resistance gene (i.e., a selectable marker), not a "gene of interest" as the instant application uses these terms. Moreover, because Peredelchuk's plasmids are intended for use only in bacteria, the *cat* gene is not "under the control of a transcription promoter and a transcription terminator active in a mammalian cell" as required by the instant claims. Thus, Applicants assert that Applicants' vectors are patentably distinct from those disclosed by Black and respectfully request that the Examiner withdraw the rejection of claims 23, 24 and 26 under § 102(b).

**The Claims Are Not Obvious**

The Examiner rejected claims 9-11, 14-16, 23, 24, 26-28, 42-44, 48, and 49 under 35 U.S.C. § 103(a) as allegedly being unpatentable over U.S. Patent Nos. 6,143,530 or 6,492,164 to Crouzet et al. as applied to claims 1-3, 6-8, 17, 19-22, 29, 30, and 34-37 above, and further in view of Backman, EP 0160571. (Office Action, page 8.)

The Examiner also rejected claims 34-38 under § 103(a) as allegedly being unpatentable over U.S. Patent Nos. 6,143,530 or 6,492,164 to Crouzet et al. as applied to claims 1-3, 6-8, 17, 19-22, 29, 30, and 34-37 above, and further in view of Bigger et al. (J. Biol. Chem. 276 (25): 23018-23027, 22 June 2001). (*Id.*)

The Examiner rejected claims 42-46 under § 103(a) as allegedly being unpatentable over U.S. Patent Nos. 6,143,530 or 6,492,164 to Crouzet et al., each further in view of Backman as applied to claims 9-11, 14-16, 23, 24, 26-28, 42-44, 48, and 49 above, and of Bigger. (*Id.*, page 9.)

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Applicants respectfully traverse these rejections. Application 09/981,803 (i.e., the instant application) and U.S. Patent Nos. 6,143,530 and 6,492,164 were, at the time the invention of Application 09/981,803 was made, all owned by Aventis Pharma S.A. Because the Examiner asserts that both U.S. Patent No. 6,143,530 and U.S. Patent No. 6,492,164 are 102(e) and/or 102(f) prior art, neither patent is available as prior art under 35 U.S.C. § 103(c). For this reason, Applicants request the withdrawal of the rejection of claims 9-11, 14-16, 23, 24, 26-28, 38, 42-46, 48, and 49 under 35 U.S.C. § 103(a). As applied to claims 34-37, which have been cancelled, these rejections are moot.

**The Double Patenting Rejections**

The Examiner rejected claims 1-3, 6-8, 17, 19-22, 29, 30, and 34-37 under the doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-18, 24, 25, and 28-37 of U.S. Patent No. 6,143,530. (Office Action, page 10.) In addition, the Examiner rejected claims 1-3, 7, and 8 under the under the doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-4 of U.S. Patent No. 6,492,164. (*Id.*, page 11.)

The cancellation of claims -3, 6-8, 17, 19-22, 29, 30, and 34-37 renders these rejections moot.

The Examiner rejected claims 9-11, 14-16, 23, 24, 26-28, 42-44, 48, and 49 as allegedly being unpatentable over claims 1-18, 24, 25, and 28-37 of U.S. Patent No. 6,143,530 in view of Backman. (*Id.*, pages 10-11.) The Examiner also rejected claims 34-38 under the doctrine of obviousness-type double patenting as allegedly being

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unpatentable over claims 34 and 37 of U.S. Patent No. 6,143,530 in view of Bigger. (*Id.*, page 11.)

The rejection of claims 34-37 for obviousness-type double patenting is moot in view of the cancellation of those claims. Applicants respectfully traverse the rejection of claim 38 over U.S. Patent No. 6,143,530 in view of Bigger. According to the M.P.E.P.,

> "The public policy behind this doctrine [double patenting] is that:
>
> > The public should . . . be able to act on the assumption that upon the expiration of the patent it will be free to use not only the invention claimed in the patent but also modifications or variants which would have been obvious to those of ordinary skill in the art at the time the invention was made, taking into account the skill in the art and prior art other than the invention claimed in the issued patent.

M.P.E.P. § 804 (quoting *In re Zickendraht*, 319 F.2d 225, 232, 138 U.S.P.Q. 22, 27 (C.C.P.A. 1963).

Therefore, it is modifications and variants that were obvious at the time the invention of the *issued patent* was made that are relevant to the double patenting inquiry. Here, the Examiner is combining a reference that appeared in the June 2001 issue of the *Journal of Biological Chemistry*, with the claims of U.S. Patent No. 6,143,530, which is entitled to a filing date no later than February 26, 1996. As a result, the invention claimed in instant claim 38 could not have been obvious in view of Bigger at the time the invention claimed in U.S. Patent No. 6,143,530 was made. Applicants respectfully request the reconsideration and withdrawal of the double patenting rejection of claim 38.

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202.408.4000
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Notwithstanding this request and solely to expedite prosecution, Applicants will file a Terminal Disclaimer over U.S. Patent No. 6,143,530 once allowable subject matter is identified.

**Conclusion**

In view of the foregoing amendments and remarks, Applicants respectfully request the reconsideration and reexamination of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: June 17, 2003

By: 
William L. Strauss
Reg. No. 47,114

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
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**APPENDIX TO AMENDMENT OF JUNE 17, 2003**
**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

Deleted text is marked by double strikethrough, and added text is underlined.

Amendments to the Specification

On page 1 (the title sheet), please replace all the text with the following:

--UNITED STATES PATENT APPLICATION FOR DNA MOLECULES, PREPARATION THEREOF AND USE THEREOF IN GENE THERAPY BY ~~Joel GROUZET, Daniel SCHERMAN,~~ Francis BLANCHE and Beatrice CAMERON~~, Pierre WILS, Anne-Marie DARQUET-DE CONTI~~--

On page 2, please replace paragraph [001] with the following:

--[001] This application is a continuation-in-part of U.S. Patent Application No. 09/655,728, filed September 5, 2000, now U.S. Patent No. 6,492,164, which ~~is~~ was a ~~continuation~~ division of U.S. Patent Application No. 08/894,511, filed August 19, 1997, now U.S. Patent No. ~~6,143,539~~ 6,143,530, which was a national stage application of PCT/FR96/00274 (not published in English), filed February 21, 1996, both of which are incorporated by reference herein.--

Amendments to the claims

4. (Amended) The molecule according to claim ~~2~~ 57, wherein said molecule is MC3909, MC3948, or MC4009.

12. (Amended) The molecule according to claim ~~10~~ 13, wherein said molecule is MC3955 or MC4007.

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13. (Amended) The molecule according to claim ~~12~~ 10, wherein the sequence that forms a triple helix and the sequence attB are contiguous and are as set forth in SEQ ID NO: 13.

24. (Amended) The plasmid according to claim 23, further comprising an origin of replication and a selection marker gene, wherein the origin of replication and selection marker gene are located outside said ~~polynucleotide~~ expression cassette.

26. (Amended) The plasmid according to claim 24, wherein the selection marker gene is a gene for kanamycin resistance or ~~a~~ the tRNA suppressor ~~(supPhe)~~ supPhe.

43. (Amended) The method according to claim 42, wherein the cultured host cell is brought into contact with the integrase and the excisionase by transforming or infecting the cultured host cell with a plasmid or a phage containing ~~at~~ a gene for at least one of the recombinase or the excisionase.

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DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
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